

FIG. 1A

					aat Asn										tca [†] Ser	*.	857
cgc Arg	tgc Cys	cgc Arg 220	agc Ser	ctg Leu	cag Gln	gag Glu	gag Glu 225	ctg Leu	tat Tyr	cta Leu	ctg Leu	aag Lys 230	cag Gln	gag Glu	ctg Leu		905
cag Gln	cga Arg 235	gcc Ala	aac Asn	atg Met	gtt Val	tcc Ser 240	tcc Ser	tgt Cys	gag Glu	ctg Leu	gaa Glu 245	ttg Leu	caa Gln	gag Glu	cag Gln		953
tcc Ser 250	ctg Leu	agg Arg	aca Thr	gcc Ala	agc Ser 255	gac Asp	cag Gln	gag Glu	tcc Ser	ggg Gly 260	gat Asp	gag Glu	gag Glu	ctg Leu	aac Asn 265		1001
					aat Asn												1049
gcg Ala	gag Glu	aag Lys	gac Asp 285	att Ile	ctg Leu	gag Glu	cag Gln	agc Ser 290	ctg Leu	gac Asp	gag Glu	gcg Ala	cgg Arg 295	ggg Gly	agc Ser		1097
cga Arg	cag Gln	gag Glu 300	ctg Leu	gtg Val	gag Glu	cgc Arg	atc Ile 305	cac His	tcg Ser	ctg Leu	cgg Arg	gag Glu 310	cgg Arg	gcc Ala	gtg Val		1145
gct Ala	gcc Ala 315	gag Glu	agg Arg	cag Gln	cga Arg	gag Glu 320	cag Gln	tac Tyr	tgg Trp	gaa Glu	gag Glu 325	aag Lys	gaa Glu	cag Gln	acc Thr		1193
					aag Lys 335												1241
aag Lys	gtg Val	aat Asn	gcg Ala	ctg Leu 350	cag Gln	gcc Ala	cag Gln	gtg Val	tgc Cys 355	gag Glu	ctg Leu	cag Gln	aag Lys	gag Glu 360	cga Arg		1289
gac Asp	cag Gln	gcg Ala	tac Tyr 365	tcc Ser	gcg Ala	agg Arg	gac Asp	agt Ser 370	gct Ala	cag Gln	agg Arg	gag Glu	att Ile 375	tcc Ser	cag Gln		1337
					gac Asp												1385
gac Asp	cag Gln 395	gtc Val	tgc Cys	gag Glu	ctg Leu	cgc Arg 400	aca Thr	cag Gln	ctt Leu	cgc Arg	cag Gln 405	ctg Leu	cag Gln	gca Ala	gag Glu		1433
cct Pro 410	ccg Pro	ggt Gly	gtg Val	ctc Leu	aag Lys 415	Gln	gaa Glu	gcc Ala	Arg	acc Thr 420	agg Arg	gag Glu	ccc Pro	tgt Cys	cca Pro 425		1481

FIG. 1B

															·	•
		_	-		ctg Leu			_		_		-		-		1529
_	_	_	_	_	ctc Leu	_	_					_		_	_	1577
				-	tcc Ser				-		-	_		_		1625
-	-				ccc Pro	-	_	_		-		_			-	1673
				_	gaa Glu 495					_	_	-	-			1721
			-	_	gga Gly	-	_	_		-	_	_		_		1769
				-	ctc Leu		_	_	_	_		_	_	_	-	1817
		-	_		gtc Val						-	_	_		_	1865
					cgg Arg											1913
					cag Gln 575											1961
					acg Thr											2009
					atg Met											2057
					tca Ser											2105
					gcc Äla		Gly		Leu	Arg						2153

FIG. 1C

																-5.* • •
					aag Lys 655											2201
cag Gln	gac Asp	ctg Leu	gag Glu	gcc Ala 670	aaa Lys	gtg Val	gcg Ala	acc Thr	tcg Ser 675	ggg Gly	gac Asp	tca Ser	ttc Phe	tac Tyr 680	atc Ile	2249
cgg Arg	gtc Val	aac Asn	ctg Leu 685	gcc Ala	atg Met	gag Glu	ggc Gly	agg Arg 690	gcc Ala	aaa Lys	ggg Gly	gag Glu	ctg Leu 695	cag Gln	gtg Val	2297
cat His	tgc Cys	aac Asn 700	gag Glu	gtc Val	ctg Leu	cac His	gtc Val 705	acc Thr	gac Asp	acc Thr	atg Met	ttc Phe 710	cag Gln	ggc Gly	tgc Cys	2345
ggc Gly	tgc Cys 715	tgg Trp	cat His	gcc Ala	cac His	cgc Arg 720	gtg Val	aac Asn	tct Ser	tac Tyr	acc Thr 725	atg Met	aag Lys	gat Asp	act Thr	2393
gcc Ala 730	gcg Ala	cac His	ggc Gly	acc Thr	atc Ile 735	ccc Pro	aac Asn	tac Tyr	tcc Ser	agg Arg 740	gct Ala	cag Gln	cag Gln	cag Gln	ctc Leu 745	2441
					gac Asp											2489
cca Pro	tct Ser	tct Ser	ggg Gly 765	gga Gly	cca Pro	cag Gln	aag Lys	ctg Leu 770	gtc Val	cgc Arg	atc Ile	gtc Val	agt Ser 775	atg Met	gac Asp	2537
aaa Lys	gcc Ala	aag Lys 780	gcc Ala	agc Ser	cct Pro	ctg Leu	cgt Arg 785	Leu	tcc Ser	ttt Phe	gac Asp	agg Arg 790	ggc Gly	cag Gln	ttg Leu	2585
gac Asp	ccc Pro 795	agc Ser	agg Arg	atg Met	gag Glu	ggc Gly 800	tcc Ser	agc Ser	acg Thr	tgc Cys	ttc Phe 805	tgg Trp	gcc Ala	gag Glu	agc Ser	2633
tgc Cys 810	Leu	acc Thr	ctg Leu	gtg Val	ccc Pro 815	tat Tyr	acc Thr	ctg Leu	gtg Val	tgg Trp 820	Pro	cat His	cga Arg	ccc Pro	gcc Ala 825	2681
cgg Arg	ccc Pro	cgg Arg	cct	gtg Val 830	Leu	ctc Leu	gtg Val	ccc	agg Arg 835	Ala	gtt Val	Gly	aag Lys	atc Ile 840	ctg Leu	2729
				Cys					Phe					Ala	gag Glu	
tac Tyr	ttg Leu	agc Ser 860	Gln	gag Glu	gag Glu	tat Tyr	gag Glu 865	ı Ala	tgg Trp	agc Ser	cag Gln	aga Arg 870	Gly	gac Asp	atc Ile	2825

FIG. 1D

			gga Gly													2873
			tcc Ser													2921
			agt Ser													2969
			gtc Val 925													3017
			cgg Arg													3065
			gag Glu													3113
			gac Asp													3161
-	_	-	atc Ile	_	Asp		_	_		Val					Gln	3209
-		cga Arg	tga *	tgc	accgt	tgc (ccct [.]	tccc	gg ga	actg	tggg	g gc	ttct	gtgt		3261
ggca aggt ttta gagg cctq gtca ccca tggq cagt	acat tcac acca ggact gaaagg aagg ccac tgtg	gag (aca (ggc - gca (gct - gct - gtg -	gccg cagt ttgg ttcc ggcc tttg ctgc ttct	gctc gaag catg catg gagt cacc cagc gtaa	to co acc to co acc to acc acc acc acc acc acc acc acc acc ac	ccacrettgaad tecces actored ac	tggc taac ctgga tatga tatga gggg gctg ctct	t gg t gc a acc gg ag c ag gg gg	ggtc acac ccct ggag gctg aggc aggc tgcc tggt	taac tttt gaga gccc cact agcg ataa tcag ggag	ctte ctg atg cgg tcc ggt gcc gaa acg	gaace tggae tttc actte gggg cacae ctcc gtac	cct aac tgc tac tac ctat tat tagt tat tagt	cacca atcta agta tgga attta ctgg gctg ttaca cagt	ctcctt acgtgc tcaccc ggacag aaaccg tgatgt gtggtc tgacgc agagac gggtct ccagta	3321 3381 3441 3501 3561 3621 3681 3741 3801 3861 3921 3931

FIG. 1E

E L C R R D S A L T A L D E E T L W... ATG GGG GAA CTG TGC CGC AGG GAC TCC GCA CTC ACG GCA CTG GAC GAG GAG ACA CTG TGG (4.60 20) R H R Ι V R CIC P GAG ATG ATG GAG AGC CAC CGC CAC AGG ATC GTA CGC TGC ATC TGC CCC AGC CGC CTC ACC K V L С Q L D Ε Ε 60 CCC TAC CTG CGC CAG GCC AAG GTG CTG TGC CAG CTG GAC GAG GAG GAG GTG CTG CAC AGC 180 Α M R Α Н G L L D L K 80 CCC CGG CTC ACC AAC AGC GCC ATG CGG GCC GGG CAC TTG CTG GAT TTG CTG AAG ACT CGA 240 F Α Α L Ε S L K F Н N 100 GGG AAG AAC GGG GCC ATC GCC TTC CTG GAG AGC CTG AAG TTC CAC AAC CCT GAC GTC TAC 300 V T G L Q P D V D F S N F S G Ε 120 ACC CTG GTC ACC GGG CTG CAG CCT GAT GTT GAC TTC AGT AAC TTT AGC GGT GAG AGC TCC 360 S N R Τ. R Τ. 140 GAC TTT GAC GGT TTG GCA GGC ACT TCT AGG AAC CTC AGG CTC CTG GTA ACC CCA GGT CTC 420 ĸ T Τ. E С L Α G Α I G 160 ATG GAG ACA TCC AAG CTG ACC GAG TGC CTG GCT GGG GCC ATC GGC AGC CTG CAG GAG GAG 480 0 Ε V L L R R С 0 180 CTG AAC CAG GAA AAG GGG CAG AAG GAG GTG CTG CGG CGG TGC CAG CAG CTG CAG GAG 540 Α E Т R E Α G L H Q L Ė 200 CAC CTG GGC CTG GCC GAG ACC CGT GCC GAG GGC CTG CAC CAG CTG GAG GCT GAC CAC AGC 600 . R S Ε V Α Η F Η E V 220 R CGC ATG AAG CGT GAG GTT AGC GCA CAC TTC CAT GAG GTG CTG AGG CTG AAG GAC GAG ATG 660 S N Α L Q E K E 240 CTC AGC CTC TCG CTG CAC TAT AGC AAT GCG CTG CAG GAG AAG GAG CTG GCC GCC TCA CGC 720 ELYLL 0 E K Q E 260 L Q R TGC CGC AGC CTG CAG GAG GAG CTG TAT CTA CTG AAG CAG GAG CTG CAG CGA GCC AAC ATG 780 E T. L Q E Q S R 280 GTT TCC TCC TGT GAG CTG GAA TTG CAA GAG CAG TCC CTG AGG ACA GCC AGC GAC CAG GAG 840 Ε Ε L N R L K Ε E N Ε K 300 L TCC GGG GAT GAG GAG CTG AAC CGC CTG AAG GAG GAG AAT GAG AAA CTG CGC TCG CTG ACT 900 K D I L Ε Q S D L Ε Α 320 TTC AGC CTG GCG GAG AAG GAC ATT CTG GAG CAG AGC CTG GAC GAG GCG CGG GGG AGC CGA 960 R Ι Н s L R Ε R Α 340 Α CAG GAG CTG GTG GAG CGC ATC CAC TCG CTG CGG GAG CGG GCC GTG GCT GCC GAG AGG CAG 1020 Α R Ρ S Ε L L S F T V H V S Н S 360 CGA GAG CAG GCC AGA CCC TCA GAG CTG CTG AGC TTC ACG GTC CAT GTG TCC CAC TCT GTC 1080 Q T L Ε L Q F Q 380 CAG TAC TGG GAA GAG AAG GAA CAG ACC CTG CTG CAG TTC CAG AAG AGT AAG ATG GCC TGC 1140 V C E R E K V NALQA Q 400 CAA CTC TAC AGG GAG AAG GTG AAT GCG CTG CAG GCC CAG GTG TGC GAG CTG CAG AAG GAG Α D S Α Q Ε R S 420 CGA GAC CAG GCG TAC TCC GCG AGG GAC AGT GCT CAG AGG GAG ATT TCC CAG AGC CTG GTG 1260 V S L Q F L T R R Ē D Q V C E 440 GAG AAG GAC TCC CTC CGC AGG CAG GTG TTC GAG CTG ACG GAC CAG GTC TGC GAG CTG CGC 1320

4,17

RQLQAEPPGVLKQ E ACA CAG CTT CGC CAG CTG CAG GCA GAG CCT CCG GGT GTG CTC AAG CAG GAA GCC AGG ACC 1380 P R E K Q R V L RMHA Ι 480 AGG GAG CCC TGT CCA CGG GAG AAG CAG CGG CTG GTG CGG ATG CAT GCC ATC TGC CCC AGA D C S L V S S T ESQLL 500 GAC GAC AGC GAC TGC AGC CTC GTC AGC TCC ACA GAG TCT CAG CTC TTG TCG GAC CTG AGT 1500 F E V R L р S R S S S P А 520 GCC ACG TCC AGC CGC GAG CTG GTG GAC AGC TTC CGC TCC AGC AGC CCC GCG CCC CCC AGC K R V Α E D FGEE 540 CAG CAG TCC CTG TAC AAG CGG GTG GCC GAG GAC TTC GGG GAA GAA CCC TGG TCT TTC AGC I P E G D P G ALPGA 560 AGC TGC CTG GAG ATC CCG GAG GGA GAC CCG GGA GCC CTG CCG GGA GCT AAG GCA GGC GAC 1680 E L L D T Α D P Q L Ε 580 L S CCA CAC CTG GAT TAT GAG CTC CTA GAC ACG GCA GAC CTT CCG CAG CTG GAA AGC AGC CTG P G R L D V s Ε 600 S A Q A CAG CCA GTC TCC CCT GGA AGG CTT GAT GTC TCG GAG AGT GCA CAA GCC GGT CGT CTC CCG 1800 V L M R R R P ARRIL 620 GCC TGC AGC GGC GTC CTC ATG CGG CGG AGG CCA GCC CGC AGG ATC CTG AGC CAG GTC ACC 1860 D Α L Ε I L Q S T G G 640 ATG CTG GCG TTC CAG GGG GAT GCA TTG CTG GAG CAG ATC AGC GTC ATC GGC GGG AAC CTC F Ι H R Т Ρ G S Α Α D 660 ACG GGC ATC TTC ATC CAC CGG GTC ACC CCG GGC TCG GCG GCG GAC CAG ATG GCC TTG CGC 1980 I V M V D Y E ASEPLFK 680 CCG GGC ACC CAG ATT GTG ATG GTT GAT TAC GAA GCC TCA GAG CCC TTG TTC AAG GCA GTC T T L Ε Ε Α V G L L R R 700 CTG GAG GAC ACG ACC CTG GAG GAG GCC GTG GGG CTT CTC AGG AGG GTG GAC GGC TTC TGC 2100 V V Т K N Đ G Y K R D 720 TGC CTG TCT GTG AAG GTC AAC ACG GAC GGT TAT AAG AGG CTA CTC CAG GAC CTG GAG GCC 2160 T S G D S F YIRVNLAM 740 AAA GTG GCG ACC TCG GGG GAC TCA TTC TAC ATC CGG GTC AAC CTG GCC ATG GAG GGC AGG 2220 Q V Н С Ε N V L H V Т Т 760 GCC AAA GGG GAG CTG CAG GTG CAT TGC AAC GAG GTC CTG CAC GTC ACC GAC ACC ATG TTC 2280 G C W Н А Н R V N S Y T M K D 780 CAG GGC TGC TGC TGG CAT GCC CAC CGC GTG AAC TCT TAC ACC ATG AAG GAT ACT GCC 2340 I P N Y S AQQQLIA R 800 GCG CAC GGC ACC ATC CCC AAC TAC TCC AGG GCT CAG CAG CTC ATA GCC CTC ATC CAG С T V 0 T R K P s s G G Р 820 GAC ATG ACT CAG CAG TGC ACC GTG ACC CGC AAG CCA TCT TCT GGG GGA CCA CAG AAG CTG 2460 V S M D K Α K Α S P L R L F 840 GTC CGC ATC GTC AGT ATG GAC AAA GCC AAG GCC AGC CCT CTG CGT TTG TCC TTT GAC AGG 2520 S R M E G S S T C F W 860 GGC CAG TTG GAC CCC AGC AGG ATG GAG GGC TCC AGC ACG TGC TTC TGG GCC GAG AGC TGC V Y T P L V R P Н R P A Р 880 R CTC ACC CTG GTG CCC TAT ACC CTG GTG CGG CCC CAT CGA CCC GCC CGG CCC GGG CCT GTG 2640 ₽ R 900 Α V G K I L S E K L С CTC CTC GTG CCC AGG GCG GTT GGG AAG ATC CTG AGC GAG AAA CTG TGC CTC CAA GGG 2700 LSQEEYEA TTT AAG AAG TGC CTG GCA GAG TAC TTG AGC CAG GAG GAG TAT GAG GCC TGG AGC CAG AGA

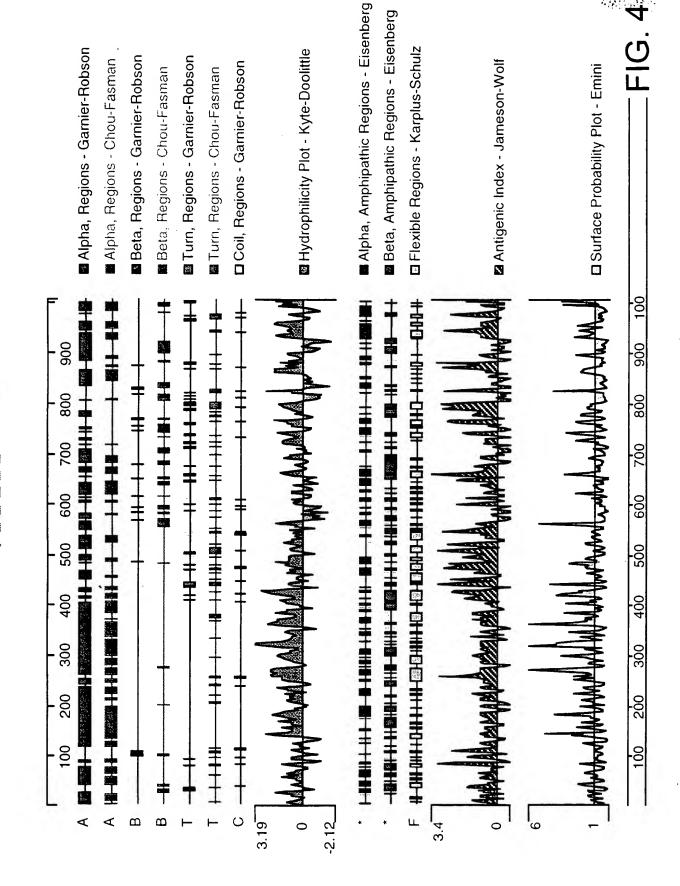
FIG. 2B

II QEGEVSGGRCWVTRH GGG GAC ATC ATC CAG GAG GGA GAG GTG TCC GGG GGC CGC TGC TGG GTG ACC CGC CAT GCT LMEKNTHALLDVQL GTG GAG TCC CTC ATG GAA AAG AAC ACC CAT GCC CTC CTG GAC GTC CAG CTG GAC AGT GTC 2880 C T L H R M D I F P I V I H V S V N 980 TGC ACC CTG CAC AGG ATG GAC ATC TTC CCC ATC GTC ATC CAC GTC TCT GTC AAC GAG AAG 2940 M A K K L K K G L Q R L G T S E E 1000 ATG GCA AAG AAG CTC AAG AAG GGC CTA CAG CGG TTG GGC ACC TCA GAG GAG CAG CTC CTG Q E E A Α R EGDLDRAPCLY S S 1020 GAG GCT GCG AGG CAG GAG GAG GGA GAC CTG GAC CGG GCG CCC TGT CTA TAC AGC AGC CTG 3060 D G W S D L D G L L S C V R Q A GCT CCT GAC GGC TGG AGC GAC CTG GAC GGC CTG CTC AGC TGT GTC CGC CAG GCC ATC GCC 3120 K · K V Q R R R H P R I N P S 1060 GAC GAG CAG AAG AAG GTG CAA CGC CGA CGT CAT CCA AGA ATT AAC CCA AGC CAG AGG ACG 3180 Q Q C H R P 1080 Т Q R R I N R Q R M GGC ATC GCC ACC CAG CAA CGC CAG TGT CAC CGA AGA ATT AAC CCA AGG CAG AGG ATG GGC 3240 RQCHRRINPSQRT 1100 ATT GCC ACC CAG CAA CGC CAG TGT CAC CGA AGA ATT AAC CCA AGC CAG AGG ACG GGC ATC 3300 \mathbf{T} 0 Q C Q C H R R I N P S Q R T G I 1120 ACC ACC CAG CAA TGC CAG TGT CAC CGA AGA ATT AAC CCA AGC CAG AGG ACG GGC ATC GCC 3360 SDTLKKDKLLPRN 1139 ATG CCT TCA TCT TCG GAC ACT CTC AAA AAA GAT AAG CTT CTG CCC AGA AAC ACC ACA 3417

FIG. 2C

washing the most be not been than the most between the washing the most been the most gk_7 Guanylate_kin PDZpdz_new SH3_2 brinzneu DNA_pol_viral_bbx S S S S S S S

FIG. 3



EETLWEMMESHRHRIVRCICPSRLTPYLRQAKVLCQLDEEEVLHSPR 62 107 *->aeddrrllrknrlellgeltlsglLdhLleknvLteeeeEkikaknt trr..dkareLiDsvqkkGnqAfqiFlqaLretdqelladlllde<-* 63 LINSAMRAGHLLDLLKTRGKNGAIAFLESLKFHNPDVYTLVTGLQ +e + +r + + +++s 1 +L+++vL + +eE++ **CARD:** domain 1 of 1, from 16 to 107: score -4.1, E = 0.94+ + +a L+D ++++G + + +F1++L+ +++ + CARD14 CARD14

FIG. 5A

629 QVTMLAF-QGDALLEQISVIGGN1tGIFIHRVTPG-SAADQMA-LRP 611 *->eitlekevkrgglGfsikggsdk..givvsevlpGsgaAeagGrLke ++t+ ++t 1 +i++ + +gi++ +v pG +aA++ L++ GDvIlsvNG.....qdvenmsheravlaikgsgg..evtLtvlRd<-612 GTQIVMVDYeaseplfkAVLEDTTLEEAVGLLRRVDGfcCLSVKVNTD **PDZ:** domain 1 of 1, from 568 to 659: score 5.3, E = 0.39+ +e+ ++e+av +++ +++ + + A + I + D 568 CARD14 CARD14

FIG. 5B

CARD14

*->eyvvAlYDyeaqnedELsFkkGDiitvleks..ddgWweGelnr.. SH3_2: domain 1 of 1, from 679 to 744: score -4.5, E = 3.8

FYIRVNLAMEGRAKGELQVHCNEVLHVTDTMfqGCGCWHAHRVNSyt 725 +y ++ + e++ +EL ++ +++++v++ ++ g w ++ ++

...tGkeGlfPsnYVeeie<-*

619

CARD14

++t G +P + ++

726 mkdraahGripnysRaQQQ

CARD14

FIG. 5C

Guanylate_kin: domain 1 of 1, from 856 to 948: score -24.2, E = 0.073 -->TRpVpRpgEvdGkdYhFVssrEemekdIaaneFlEygefqgnyYGTs

+++s Ee e+ ++++ + ge++g +

--A------EYLS-QEEYEAWSQRGDIIQEGEVSGGRCWVT 887 856

letvrqvakqgKiciLDvepQgvkrlrtaelsNPivvFlaPpSl..qele +++v+ ++++LDv ++ v 1 + Piv+ +

888 RHAVESLMEKNTHALLDVQLDSVCTLHRMDIF-PIVIHVSVNEKmaKKLK krLegrnkesEes<-* CARD14

k L+++++ sEe+ 014 937 KGLQRLGT-SEEQ 948

FIG. 5D

the first that that the first to the natural of the first that the first that the natural of the first that the first that the natural of the first that the

*->dsyqkssgnss..lwesnyqnwqqEaaKLkaqienLQnNrnqRhllG K-box: domain 1 of 1, from 239 to 325: score -36.5, E = 2.9

S+ ++++ ++ +S++++ +E++LK+++e+L+ + 239

CARD14

VSSCELELQEQS1RTASDQESGDEELNRLKEENEKLR--SL---- 277

EdLgsLslKELqqLEqqLEkgLkhIRsrKnqllldqieelqkKErelqee R + + 1+ 1+ 1+ 1+ + + + + + sl E LEG L+++

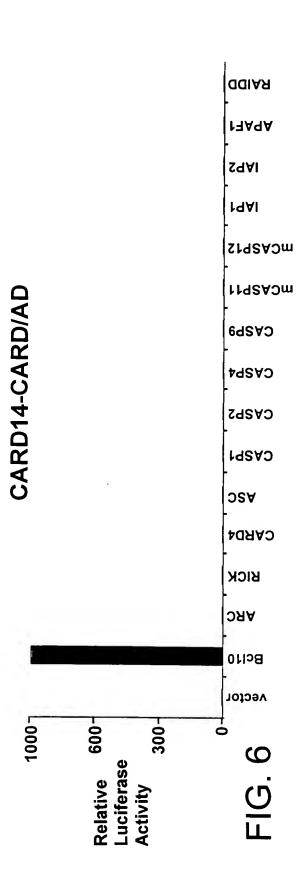
----TFSLAEKDILEQSLDEA----RGSRQE-LVERIHSLRERAVAAERQ 318 278 CARD14

NkaLrkKiee<-*

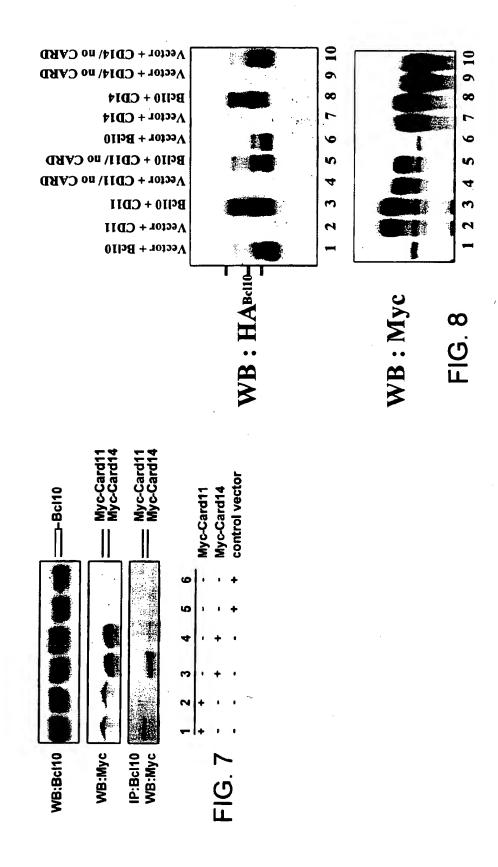
+ + +ee 319 RE---QYWEE

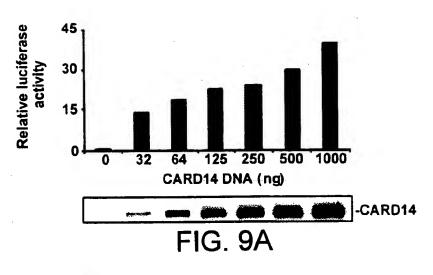
CARD14

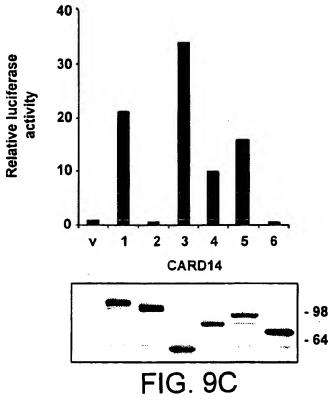
FIG. 5E



- Marin aris







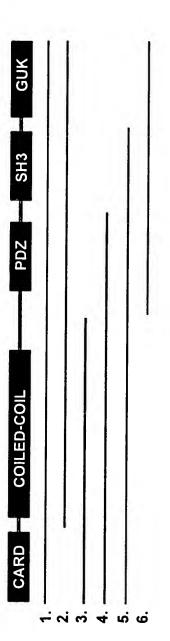


FIG. 9B